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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,779	07/03/2001	Kent D. Taylor	18810-82302	6070

7590 06/06/2002

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555 West Fifth Street
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EXAMINER
GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
1634	#9

DATE MAILED: 06/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/898,779	Applicant(s) TAYLOR ET AL.	
	Examiner Jeanine A Goldberg	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *84-86,89,91-93, 95-117* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *84-86,89,91-93 and 95-117* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed May 6, 2002. Currently, claims 84-86, 89, 91-93, 95-117. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

2. Any objections and rejections not reiterated below are hereby withdrawn.

3. This action contains new grounds of rejection necessitated by amendment.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 89 and 95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glock et al (J. or Forensic Sciences, Vol. 41, no. 4, pg. 579-581, July 1996) or Takagi et al (Molecular and Cellular Probes, Vol. 10, pg. 227-228,1996) or Zuliani et al (Nucleic Acids Research, Vol. 18, no 16, pg. 4958, 1990) or Ahn (J. of Lipid Research, Vol. 34, pg. 421-428, 1993) in view of Nickerson (Nature Genetics, Vol. 19, no. 3, pg. 233-240, July 1999; Genbank Accession No. AF050163, September 1998).

This rejection encompasses oligonucleotides which amplify part of intron 6. "having a nucleotide sequencing consisting of" language is read as open language indicating that the claims are drawn to sequences which contain the SEQ ID NO and any additional nucleotides on either side of the sequence. The intended use in the preamble of product claims carries no patentable weight.

Glock teaches oligonucleotide primers which amplify intron 6 of the lipoprotein lipase gene which are identical to SEQ ID NO: 33 and SEQ ID NO: 34 (pg. 579, col. 2, para. 3). The primers disclosed in Glock, 5'- ATCTGACAAGGATAGTGGGATATA-3' (forward primer- TTTA strand) and 5'-CCTGGGTAACTGAGCGAGACTGTGTC-3' (reverse primer-TAAA) are 100% identical to the primers of the instant claims. Additional SEQ ID NO: 87 and 91 of the instant application overlap these primers.

Takagi teaches oligonucleotide primers which amplify intron 6 of the lipoprotein lipase gene which are identical to SEQ ID NO: 37 and SEQ ID NO; 38 (pg. 227). The primers disclosed in Takagi, 5'- ATCTGACAAGGATAGTGGGATATA-3' and 5'-CCTGGGTAACTGAGCGAGACTGTGTC-3' are 100% identical to the primers of the instant claims. Additional SEQ ID NO: 87 and 91 of the instant application overlap these primers.

Zuilani teaches oligonucleotide primers which amplify intron 6 of the lipoprotein lipase gene which are identical to SEQ ID NO: 37 and SEQ ID NO; 38 (pg. 4958, col. 2). The primers disclosed in Zuilani, 5'- ATCTGACAAGGATAGTGGGATATA-3' and 5'-CCTGGGTAACTGAGCGAGACTGTGTC-3' are 100% identical to the primers of the

instant claims. Additional SEQ ID NO: 87 and 91 of the instant application overlap these primers.

Ahn teaches a primer pair which is designed to amplify a PvuII restriction site in intron 6. The primer pair of Ahn amplifies the newly identified TTTA repeat region.

Niether Glock, Takagi, Zuliani nor Ahn specifically teach all of the primer permutations of the instant claims.

However, Nickerson et al. (herein referred to as Nickerson) teaches the sequence of the human lipoprotein lipase gene. Nickerson also provides two positions for sequence variants within intron 6 of the sequence.

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have modified the primers of either Glock, Takagi, Ahn, or Zuliani with the teachings of Nickerson. Since the sequence of exon 6, intron 6, as well as the full length LPL gene, was known as provided by Nickerson, the ordinary artisan would have been motivated to amplify the region of intron 6 to detect the disclosed polymorphism. The TTTA polymorphism was known in the art at the time the invention was made. The ordinary artisan would have been motivated to have optimized primer selection within the intron around the TTTA polymorphism to obtain optimal results. Further, in the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologues, however, the court stated

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed primers simply represent functional equivalents of the primer pairs provided by Ahren, Takagi, Zuliani, or Glock, the ordinary artisan would have been motivated to have obtained alternative primers, homologues, for amplification of the known polymorphism within intron 6. Any primer pairs which flank the known polymorphism would serve as functional equivalents of the known primer pairs which flank the polymorphism. Since the full length disclosed nucleic acid sequence of the LPL gene concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references.

Response to Arguments

The response traverses the rejection. The response asserts that the claims have been amended to overcome the rejection by amending the claims to recited a "primer having a nucleotide sequence consisting of". This amendment to the claims has not changed the scope of the claims. Having is read to encompass comprising language.

The response appears to believe that the rejection was drawn to only SEQ ID NO: 33, 34, 87 and 91, however, as set out at the beginning of the rejection and reiterated in the response, "this rejection encompasses oligonucleotides which amplify

part of intron 6." Therefore, the rejection is still applicable to functional equivalents, which function to amplify part of intron 6, namely the known polymorphism. The specification teaches that SEQ ID NO: 82-92 amplify nucleic acids sequences including the TTTAn tetranuceotide repeat region in intron 6, the known polymorphism. Therefore modifying known primers which flank the known polymorphism to obtain functional equivalents for amplifying nucleic acids contain the known polymorphism would have been obvious.

Thus for the reasons above and those already of record, the rejection is maintained.

5. Claims 84-86, 92-93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gotoda (Journal of Lipid Res. Vol. 33, no. 7, pg. 1067-1072, 1992) or Ahn (J. of Lipid Research, Vol. 34, pg. 421-428, 1993) in view of Nickerson (Nature Genetics, Vol. 19, no. 3, pg. 233-240, July 1999; Genbank Accession No. AF050163, September 1998).

This rejection encompasses oligonucleotides which amplify intron 8 polymorphism HindIII. "Having a nucleotide sequencing consisting of" language is read as open language indicating that the claims are drawn to sequences which contain the SEQ ID NO and any additional nucleotides on either side of the sequence. The intended use in the preamble of product claims carries no patentable weight.

Gotoda et al. (herein referred to as Gotoda) teaches three DNA polymorphisms in the human lipoprotein lipase gene. Within intron 8, a T-G transversion occurs within a Hind II site. Gotoda also teaches Primer E and Primer F which function to amplify Intron 8. Primer E and Primer F and provided in Table 1 amplify intron 8.

Ahn teaches forward and reverse primers for the explicit purpose of amplifying the sequence around a HindIII restriction site in intron 8. These primers are located in the regions flanking both the 5' and 3' end of the intron. The disclosed forward primer corresponds to nucleotides 7724-7744 and the reverse primer to nucleotides 8945-8963 of the Nickerson reference.

Neither Gotoda nor Ahn specifically teach all of the primer permutations of the instant claims.

However, Nickerson et al. (herein referred to as Nickerson teaches the sequence of the human lipoprotein lipase gene. Nickerson also provides five sequence variants within intron 8 of the sequence.

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have modified the primers of Gotoda or Ahn with the teachings of Nickerson. Since the sequence of Intron 8, was known, the teachings in Nickerson and Gotoda of polymorphisms in intron 8 would have motivated the ordinary artisan to amplify the region of intron 8 flanking the HindIII polymorphism. The ordinary artisan would have further been motivated to have optimized primer selection of intron to obtain optimal results. Further, in the recent court decision *In Re*

Deuel 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologues, however, the court stated

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed primers simply represent functional equivalents of the primers of Gotoda and Ahn which amplify the HindIII polymorphism within intron 8. The art provides at least two pairs of primers which function to amplify the HindIII polymorphism, namely the primers of Gota E and F and the primers of Ahn. Any primer pairs which flank the known polymorphism would serve as functional equivalents of the known primer pairs which flank the polymorphism. The full length disclosed nucleic acid sequence of the LPL gene has been provided such that a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references.

Response to Arguments

The response traverses the rejection. With respect to Claims 84-85, the response asserts that the claims have been amended to overcome the rejection by amending the claims to recited a "primer having a nucleotide sequence consisting of". This amendment to the claims has changed, i.e. broadened, the scope of the claims.

With respect to Claims 86, 92-92, the response asserts that the claims have been amended to overcome the rejection by amending the claims to recited a "primer having a nucleotide sequence consisting of". This amendment to the claims has not changed the scope of the claims. Having is read to encompass comprising language.

It is noted that "this rejection encompasses oligonucleotides which amplify intron 8 polymorphism HindIII." Therefore, the rejection is applicable to functional equivalents, which function to amplify part of intron 8, HindIII polymorphism, namely the known polymorphism. The specification teaches that SEQ ID NO: 1-32, 35-79 amplify nucleic acids sequences including the HindIII region in intron 8, the known polymorphism. Therefore modifying known primers which flank the known polymorphism to obtain functional equivalents for amplifying nucleic acids contain the known polymorphism would have been obvious.

Thus for the reasons above and those already of record, the rejection is maintained.

6. Claims 91 and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paulweber et al (Artherosclerosis, Vol. 86, pg. 239-250, 1991) in view of Oka (Biochim. Biophys. Acta, Vol. 1049, no. 1, pg. 21-26, 1990; Genbank Accession No. X52978, November 1992).

This rejection encompasses oligonucleotides of the 3' UTR region, namely SEQ ID NO: 100-111. "Having a nucleotide sequencing consisting of" language is read as

open language indicating that the claims are drawn to sequences which contain the SEQ ID NO and any additional nucleotides on either side of the sequence. The intended use in the preamble of product claims carries no patentable weight.

Paulweber et al. (herein referred to as Paulweber) teaches several primers which are used to amplify the 3'UTR region of exon 10 (pg. 242, Figure 1). The position of the primers are provided in Table 2 (pg. 245)

Paulweber does not specifically teach the primer permutations of the instant claims.

However, Oka teaches the 3'UTR region and intron 10. Oka further teaches the gene sequence of exon 10 contains the entire 3' untranslated sequence and the potential polyadenylation sequences are 390 base pairs apart.

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have designed primers, as taught by Paulweber, for the 3'UTR region, as taught by Oka, of the lipoprotein lipase gene. Since the sequence of the 3'UTR region was known, as taught by Oka, and the ordinary artisan would have been motivated to amplify the region of the 3'UTR region to detect the region, the gene, or to use the primer in combination with a primer at the most 5' region of the gene for amplification of the entire gene. The ordinary artisan would have further been motivated to have optimized primer selection within the region to obtain optimal results. Further, in the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of

identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologues, however, the court stated

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

The claimed primers simply represent structural and functional homologues of the full length disclosed nucleic acid sequence of the LPL gene concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited reference in the absence of secondary considerations.

Response to Arguments

The response traverses the rejection. With respect to Claims 91, 96, the response asserts that the claims have been amended to overcome the rejection by amending the claims to recited a "primer having a nucleotide sequence consisting of". This amendment to the claims has not changed the scope of the claims. Having is read to encompass comprising language.

It is noted that "this rejection encompasses oligonucleotides which amplify 3' UTR region." Therefore, the rejection is applicable to functional equivalents, which function to amplify the known 3' UTR region. The specification teaches that SEQ ID NO: 95-106 amplify nucleic acids sequences including the exon 10 and the 3' UTR.

Therefore modifying known primers which flank the known polymorphism to obtain functional equivalents for amplifying nucleic acids contain the known polymorphism would have been obvious.

Thus for the reasons above and those already of record, the rejection is maintained.

7. Claims 97 and 100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gotoda (Journal of Lipid Res. Vol. 33, no. 7, pg. 1067-1072, 1992) or Ahn (J. of Lipid Research, Vol. 34, pg. 421-428, 1993) in view of Nickerson (Nature Genetics, Vol. 19, no. 3, pg. 233-240, July 1999; Genbank Accession No. AF050163, September 1998) as applied to Claims 84-86, 92-93 above and further in view of Stratagene Catalog (1988).

It is noted, with regard to the limitation that the kits contain instructions for detection of a predisposition for non-responsiveness to treatment with a statin drug, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit.

Neither Nickerson, Gotoda nor Ahn specifically teach a genetic testing kit.

However, Stratagene teaches gene characterization kits which help explore identified gene. The kits provide reagents which have been assembled and pre-mixed

and serve as a quality control. Further, the kits can save "weeks of costly and frustrating trouble-shooting".

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have packaged the primers of Gotoda or Ahn in view of Nickerson in kits as taught by Stratagene for the expected benefit of convenience and cost-effectiveness of practitioners in the art wishing to analyze intron 8 HindIII polymorphism of the lipase gene.

Response to Arguments

The response traverses the rejection. With respect to Claims 84-85, the response asserts that the claims have been amended to overcome the rejection by amending the claims to recited a "primer having a nucleotide sequence consisting of". This amendment to the claims has changed, i.e. broadened, the scope of the claims. With respect to Claims 86, 92-92, the response asserts that the claims have been amended to overcome the rejection by amending the claims to recited a "primer having a nucleotide sequence consisting of". This amendment to the claims has not changed the scope of the claims. Having is read to encompass comprising language.

It is noted that "this rejection encompasses oligonucleotides which amplify intron 8 polymorphism HindIII." Therefore, the rejection is applicable to functional equivalents, which function to amplify part of intron 8, HindIII polymorphism, namely the known polymorphism. The specification teaches that SEQ ID NO: 1-32, 35-79 amplify nucleic acids sequences including the HindIII region in intron 8, the known polymorphism.

Therefore modifying known primers which flank the known polymorphism to obtain functional equivalents for amplifying nucleic acids contain the known polymorphism would have been obvious.

The response asserts that "the legal principal is well established that 'printed matter may well constitute structural limitations upon which Patentability can be predicated,' in consideration of all the claim limitations taken as a whole. (In re Gulack, 217 USPQ, at 403, end of footnote 8). This argument has been reviewed and found non-persusasive because the court in Gulack agreed with the In Re Miller where the "board as not giving the printed matter patentable weight because the board felt that there is no functional relationship between the printed matter and the substrate". This is not support for printed matter as a structural limitation. In the case of In re Gulack, the printed matter is considered a patentable distinction because the function of the device depends upon the printed matter itself, which is a part of the substrate; without the printed indicia or numbers, the substrates lose their function. Such is not the case with the instantly claimed kit. The components of the kit remain fully functional absent the printed instructions for use. Thus the instructions for use included in a kit or article of manufacture constitute "intended use" for that kit or article of manufacture. Intended used does not impart patentable weight to a product. See MPEP 2111.03:

> Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must

result in a manipulative difference as compared to the prior art. In re Casey 370 F.2d 576, 152 USPQ 235 (CCPA 1967); In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459, (CCPA 1963).

In the instant case, the claims are drawn to a kit comprising instructions, and specific SEQ ID NO: primers. The intended use which is recited on the instructions lacks a functional relationship to the kit because the instructions do not physically or chemically affect the chemical nature of the components of the kit, and furthermore, the components of the kit can still be used by the skilled artisan for other purposes (as a whole or individually). Therefore, the kit is unpatentable over the prior art because they function equally effectively with or without the instructions, and accordingly no functional relationship exists between the instructions for use and the kit components.

In the Opinion Text of *In re Haller*, 73 USPQ 403 (CCPA 1947), the court stated "Whether the statement of intended use appears merely in the claim or in a label on the product is immaterial so far as the question of patentability is concerned." The instructions of the instant kit are not considered to distinguish the claimed kits over the prior art. In re Haller states that, in accordance with the patent statutes, an article or composition of matter, in order to be patentable, must not only be useful and involve invention, but must also be new. *If there is no novelty in an article or composition itself, then a patent cannot be properly granted on the article or composition, regardless of the use for which it was intended.* The difficulty is not that there can never be invention in discovering a new process involving the use of an old article, but that the statutes make no provision for patenting of an article or composition which is not, in and of itself, new.

Thus for the reasons above and those already of record, the rejection is maintained.

8. Claims 98 and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glock et al (J. or Forensic Sciences, Vol. 41, no. 4, pg. 579-581, July 1996) or Takagi et al (Molecular and Cellular Probes, Vol. 10, pg. 227-228,1996) or Zuliani et al (Nucleic Acids Research, Vol. 18, no 16, pg. 4958, 1990) or Ahn (J. of Lipid Research, Vol. 34, pg. 421-428, 1993) in view of Nickerson (Nature Genetics, Vol. 19, no. 3, pg. 233-240, July 1999; Genbank Accession No. AF050163, September 1998) as applied to Claims 89 and 95 above and further in view of Stratagene (1988).

It is noted, with regard to the limitation that the kits contain instructions for detection of a predisposition for non-responsiveness to treatment with a statin drug, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit.

Neither Nickerson, Glock, Takagi, Ahn nor Zuliani specifically teach a genetic testing kit.

However, Stratagene teaches gene characterization kits which help explore identified gene. The kits provide reagents which have been assembled and pre-mixed and serve as a quality control. Further, the kits can save "weeks of costly and frustrating trouble-shooting".

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have packaged the primers of Glock, Takagi, Ahn or Zuliani in kits as taught by Stratagene for the expected benefit of convenience and cost-effectiveness of practitioners in the art wishing to analyze intron 6 of the lipase gene.

Response to Arguments

The response traverses the rejection. The response asserts that the claims have been amended to overcome the rejection by amending the claims to recited a "primer having a nucleotide sequence consisting of". This amendment to the claims has not changed the scope of the claims. Having is read to encompass comprising language.

The response appears to believe that the rejection was drawn to only SEQ ID NO: 33, 34, 87 and 91, however, as set out at the beginning of the rejection and reiterated in the response, "this rejection encompasses oligonucleotides which amplify part of intron 6." Therefore, the rejection is still applicable to functional equivalents, which function to amplify part of intron 6, namely the known polymorphism. The specification teaches that SE QID NO: 82-92 amplify nucleic acids sequences including the TTTAn tetranuceotide repeat region in intron 6, the known polymorphism. Therefore modifying known primers which flank the known polymorphism to obtain functional equivalents for amplifying nucleic acids contain the known polymorphism would have been obvious.

The response asserts that "the legal principal is well established that 'printed matter may well constitute structural limitations upon which Patentability can be predicated,' in consideration of all the claim limitations taken as a whole. (In re Gulack, 217 USPQ, at 403, end of footnote 8). This argument has been reviewed and found non-persusasive because the court in Gulack agreed with the In Re Miller where the "board as not giving the printed matter patentable weight because the board felt that there is no functional relationship between the printed matter and the substrate". This is not support for printed matter is a structural limitation. In the case of In re Gulack, the printed matter is considered a patentable distinction because the function of the device depends upon the printed matter itself, which is a part of the substrate; without the printed indicia or numbers, the substrates lose their function. Such is not the case with the instantly claimed kit. The components of the kit remain fully functional absent the printed instructions for use. Thus the instructions for use included in a kit or article of manufacture constitute "intended use" for that kit or article of manufacture. Intended used does not impart patentable weight to a product. See MPEP 2111.03:

> Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey 370 F.2d 576, 152 USPQ 235 (CCPA 1967); In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459, (CCPA 1963).

In the instant case, the claims are drawn to a kit comprising instructions, and specific SEQ ID NO: primers. The intended use which is recited on the instructions lacks a

functional relationship to the kit because the instructions do not physically or chemically affect the chemical nature of the components of the kit, and furthermore, the components of the kit can still be used by the skilled artisan for other purposes (as a whole or individually). Therefore, the kit is unpatentable over the prior art because they function equally effectively with or without the instructions, and accordingly no functional relationship exists between the instructions for use and the kit components.

In the Opinion Text of *In re Haller*, 73 USPQ 403 (CCPA 1947), the court stated "Whether the statement of intended use appears merely in the claim or in a label on the product is immaterial so far as the question of patentability is concerned." The instructions of the instant kit are not considered to distinguish the claimed kits over the prior art. In re Haller states that, in accordance with the patent statutes, an article or composition of matter, in order to be patentable, must not only be useful and involve invention, but must also be new. *If there is no novelty in an article or composition itself, then a patent cannot be properly granted on the article or composition, regardless of the use for which it was intended.* The difficulty is not that there can never be invention in discovering a new process involving the use of an old article, but that the statutes make no provision for patenting of an article or composition which is not, in and of itself, new.

Thus for the reasons above and those already of record, the rejection is maintained.

9. Claims 99 and 102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paulweber et al (Artherosclerosis, Vol. 86, pg. 239-250, 1991) in view of Oka (Biochim. Biophys. Acta, Vol. 1049, no. 1, pg. 21-26, 1990; Genbank Accession No. X52978, November 1992) as applied to Claims 91 and 96 above and further in view of Stratagene Catalog (1988).

It is noted, with regard to the limitation that the kits contain instructions for detection of a predisposition for non-responsiveness to treatment with a statin drug, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit.

Neither Oka nor Paulweber specifically teaches a genetic testing kit.

However, Stratagene teaches gene characterization kits which help explore identified gene. The kits provide reagents which have been assembled and pre-mixed and serve as a quality control. Further, the kits can save "weeks of costly and frustrating trouble-shooting".

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have packaged the primers of Oka and Paulweber in kits as taught by Stratagene for the expected benefit of convenience and cost-effectiveness of practitioners in the art wishing to analyze the 3'-UTR region of the lipase gene.

Response to Arguments

The response traverses the rejection. With respect to Claims 91, 96, the response asserts that the claims have been amended to overcome the rejection by amending the claims to recited a "primer having a nucleotide sequence consisting of". This amendment to the claims has not changed the scope of the claims. Having is read to encompass comprising language.

It is noted that "this rejection encompasses oligonucleotides which amplify 3' UTR region." Therefore, the rejection is applicable to functional equivalents, which function to amplify the known 3' UTR region. The specification teaches that SEQ ID NO: 95-106 amplify nucleic acids sequences including the exon 10 and the 3' UTR. Therefore modifying known primers which flank the known polymorphism to obtain functional equivalents for amplifying nucleic acids contain the known polymorphism would have been obvious.

The response asserts that "the legal principal is well established that 'printed matter may well constitute structural limitations upon which Patentability can be predicated,' in consideration of all the claim limitations taken as a whole. (In re Gulack, 217 USPQ, at 403, end of footnote 8). This argument has been reviewed and found non-persusasive because the court in Gulack agreed with the In Re Miller where the "board as not giving the printed matter patentable weight because the board felt that there is no functional relationship between the printed matter and the substrate". This is not support for printed matter is a structural limitation. In the case of In re Gulack, the printed matter is considered a patentable distinction because the function of the device

depends upon the printed matter itself, which is a part of the substrate; without the printed indicia or numbers, the substrates lose their function. Such is not the case with the instantly claimed kit. The components of the kit remain fully functional absent the printed instructions for use. Thus the instructions for use included in a kit or article of manufacture constitute "intended use" for that kit or article of manufacture. Intended used does not impart patentable weight to a product. See MPEP 2111.03:

> Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey 370 F.2d 576, 152 USPQ 235 (CCPA 1967); In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459, (CCPA 1963).

In the instant case, the claims are drawn to a kit comprising instructions, and specific SEQ ID NO: primers. The intended use which is recited on the instructions lacks a functional relationship to the kit because the instructions do not physically or chemically affect the chemical nature of the components of the kit, and furthermore, the components of the kit can still be used by the skilled artisan for other purposes (as a whole or individually). Therefore, the kit is unpatentable over the prior art because they function equally effectively with or without the instructions, and accordingly no functional relationship exists between the instructions for use and the kit components.

In the Opinion Text of *In re Haller*, 73 USPQ 403 (CCPA 1947), the court stated "Whether the statement of intended use appears merely in the claim or in a label on the product is immaterial so far as the question of patentability is concerned." The

instructions of the instant kit are not considered to distinguish the claimed kits over the prior art. In re Haller states that, in accordance with the patent statutes, an article or composition of matter, in order to be patentable, must not only be useful and involve invention, but must also be new. *If there is no novelty in an article or composition itself, then a patent cannot be properly granted on the article or composition, regardless of the use for which it was intended.* The difficulty is not that there can never be invention in discovering a new process involving the use of an old article, but that the statutes make no provision for patenting of an article or composition which is not, in and of itself, new.

Thus for the reasons above and those already of record, the rejection is maintained.

New Grounds of Rejection Necessitated by Amendment

10. Newly added Claims 106, 110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glock et al (J. or Forensic Sciences, Vol. 41, no. 4, pg. 579-581, July 1996) or Takagi et al (Molecular and Cellular Probes, Vol. 10, pg. 227-228,1996) or Zuliani et al (Nucleic Acids Research, Vol. 18, no 16, pg. 4958, 1990) or Ahn (J. of Lipid Research, Vol. 34, pg. 421-428, 1993) in view of Nickerson (Nature Genetics, Vol. 19, no. 3, pg. 233-240, July 1999; Genbank Accession No. AF050163, September 1998) as applied to Claims 89 and 95 above, and further in view of Levenson et al. (PCR Protocols, Chapter 13, pages 99-112, 1990).

Niether Glock, Takagi, Zuliani, Ahn, nor Nickerson specifically teach labeling the primer with a fluorescent dye.

However, Levenson teaches labels may be incorporated directly into the PCR product via modified nucleoside triphosphates or primers that are labeled at their 5' termini. Levenson teaches that the "most commonly employed 5' terminal labels are biotin and a variety of fluorescent dyes.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the primers of Glock, Takagi, Zuliani and Ahn in view of Nickerson to incorporate a fluoresent dye for the express benefit of labeling the resulting PCR product. Labeled PCR products allow for detection and conformation that the nucleic acid is present in a sample.

11. Newly added Claims 103-105, 108-109 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gotoda (Journal of Lipid Res. Vol. 33, no. 7, pg. 1067-1072, 1992) or Ahn (J. of Lipid Research, Vol. 34, pg. 421-428, 1993) in view of Nickerson (Nature Genetics, Vol. 19, no. 3, pg. 233-240, July 1999; Genbank Accession No. AF050163, September 1998) as applied to Claims 84-86, 92-93 above and further in view of Levenson et al. (PCR Protocols, Chapter 13, pages 99-112, 1990).

Niether Gotoda, Ahn, nor Nickerson specifically teach labeling the primer with a fluorescent dye.

However, Levenson teaches labels may be incorporated directly into the PCR product via modified nucleoside triphosphates or primers that are labeled at their 5'

termini. Levenson teaches that the "most commonly employed 5' terminal labels are biotin and a variety of fluorescent dyes.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the primers of Gotoda, and Ahn in view of Nickerson to incorporate a fluoresent dye for the express benefit of labeling the resulting PCR product. Labeled PCR products allow for detection and conformation that the nucleic acid is present in a sample.

12. Newly added Claims 107, 111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paulweber et al (Artherosclerosis, Vol. 86, pg. 239-250, 1991) in view of Oka (Biochim. Biophys. Acta, Vol. 1049, no. 1, pg. 21-26, 1990; Genbank Accession No. X52978, November 1992) as applied to Claims 91, 96 above and further in view of Levenson et al. (PCR Protocols, Chapter 13, pages 99-112, 1990).

Niether Paulweber nor Oka specifically teach labeling the primer with a fluorescent dye.

However, Levenson teaches labels may be incorporated directly into the PCR product via modified nucleoside triphosphates or primers that are labeled at their 5' termini. Levenson teaches that the "most commonly employed 5' terminal labels are biotin and a variety of fluorescent dyes.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the primers of Paulweber in view of Oka to incorporate a fluoresent

dye for the express benefit of labeling the resulting PCR product. Labeled PCR products allow for detection and conformation that the nucleic acid is present in a sample.

13. Newly added Claims 112, 115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gotoda (Journal of Lipid Res. Vol. 33, no. 7, pg. 1067-1072, 1992) or Ahn (J. of Lipid Research, Vol. 34, pg. 421-428, 1993) in view of Nickerson (Nature Genetics, Vol. 19, no. 3, pg. 233-240, July 1999; Genbank Accession No. AF050163, September 1998) and further in view of Stratagene Catalog (1988) as applied to Claims 97, 100 above and further in view of Levenson et al. (PCR Protocols, Chapter 13, pages 99-112, 1990).

Niether Gotoda, Ahn, nor Nickerson specifically teach labeling the primer with a fluorescent dye.

However, Levenson teaches labels may be incorporated directly into the PCR product via modified nucleoside triphosphates or primers that are labeled at their 5' termini. Levenson teaches that the "most commonly employed 5' terminal labels are biotin and a variety of fluorescent dyes.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the primers of Gotoda, and Ahn in view of Nickerson to incorporate a fluoresent dye for the express benefit of labeling the resulting PCR product. Labeled

PCR products allow for detection and conformation that the nucleic acid is present in a sample.

14. Newly added Claims 113, 116 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glock et al (J. or Forensic Sciences, Vol. 41, no. 4, pg. 579-581, July 1996) or Takagi et al (Molecular and Cellular Probes, Vol. 10, pg. 227-228,1996) or Zuliani et al (Nucleic Acids Research, Vol. 18, no 16, pg. 4958, 1990) or Ahn (J. of Lipid Research, Vol. 34, pg. 421-428, 1993) in view of Nickerson (Nature Genetics, Vol. 19, no. 3, pg. 233-240, July 1999; Genbank Accession No. AF050163, September 1998) further in view of Stratagene (1988) as applied to Claims 98 and 101 above and further in view of Levenson et al. (PCR Protocols, Chapter 13, pages 99-112, 1990).

Niether Glock, Takagi, Zuliani, Ahn, nor Nickerson specifically teach labeling the primer with a fluorescent dye.

However, Levenson teaches labels may be incorporated directly into the PCR product via modified nucleoside triphosphates or primers that are labeled at their 5' termini. Levenson teaches that the "most commonly employed 5' terminal labels are biotin and a variety of fluorescent dyes.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the primers of Glock, Takagi, Zuliani, Ahn, in view of Nickerson to incorporate a fluoresent dye for the express benefit of labeling the resulting PCR

product. Labeled PCR products allow for detection and conformation that the nucleic acid is present in a sample.

15. Newly added Claims 114, 117 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paulweber et al (Artherosclerosis, Vol. 86, pg. 239-250, 1991) in view of Oka (Biochim. Biophys. Acta, Vol. 1049, no. 1, pg. 21-26, 1990; Genbank Accession No. X52978, November 1992) as applied to Claims 91 and 96 above further in view of Stratagene (1988) as applied to Claims 99, 102 above and further in view of Levenson et al. (PCR Protocols, Chapter 13, pages 99-112, 1990).

Niether Paulweber nor Oka specifically teach labeling the primer with a fluorescent dye.

However, Levenson teaches labels may be incorporated directly into the PCR product via modified nucleoside triphosphates or primers that are labeled at their 5' termini. Levenson teaches that the "most commonly employed 5' terminal labels are biotin and a variety of fluorescent dyes.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the primers of Paulweber in view of Oka to incorporate a fluoresent dye for the express benefit of labeling the resulting PCR product. Labeled PCR products allow for detection and conformation that the nucleic acid is present in a sample.

Conclusion

16. No claims allowable over the art.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of formal matters can be directed to the patent analyst, Pauline Farrier, whose telephone number is (703) 305-3550.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J Goldberg

Jeanine Goldberg
May 31, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600